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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,498	06/07/2006	Siegfried Ansorge	013183.00055	1382

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,498	ANSORGE ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-17 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-4, drawn to a method for inhibiting proliferation (DNA synthesis) comprising utilizing inhibitors of dipeptidyl peptidase IV DP IV) as well as of inhibitors of enzymes having an equal substrate specificity (DP IV-analogous enzyme activity) or/and of inhibitors of alanyl aminopeptidase (APN) as well as of inhibitors of enzymes having an equal substrate specificity (APN-analogous enzyme activity) for an inhibition of the proliferation (DNA synthesis).

Group II, claim(s) 5 and 13-14, drawn to a method of prevention and therapy of benign fibrotic and sclerotic diseases, as well as malign fibroblast hyperproliferation states, or fibrotic autoimmune diseases, or dermatosclerosis and of heterogeneous group of pseudosclerodermiae by utilizing the inhibitor combinations.

Group III, claim(s) 6-12 and 15-17, drawn to a pharmaceutical preparation, comprising inhibitors of DP IV as well as inhibitors of enzymes having DP IV-analogous enzyme activity or/and inhibitors of alanyl aminopeptidase (APN) as well as inhibitors of enzymes having APN-analogous enzyme activity, in combination with per se known carrier, additive and/or auxiliary substances.

2. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of the instant application is a method of inhibiting DAN synthesis comprising inhibitors of DP IV or DP IV-analog or/and inhibitors of APN or inhibitors of APN-analogs. Ansorge et al (US Patent # 7229969) teaches a method for producing in an individual a more than additive to superadditive inhibition of the activation, DNA synthesis, and proliferation comprising the administering to an individual an effective amount of a composition comprising an inhibitor of DP IV as well as of enzymes having

the same substrate specificity (DP IV-analogous enzymatic activity) in combination with an inhibitor of APN and or enzymes having the same substrate specificity (APN-analogous enzymatic activity) (see claims 1-12). Since the active method steps are the same (patient, active agent(s) and dosage), this prior art teaches the same special technical feature as the instant application.

3. Furthermore, the inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: DP IV inhibitors lack common structural feature.

4. The situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical) is also governed by PCT Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

5. When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and

(B)

(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or

(B)

(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

6. In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

7. In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

8. The DP IV inhibitors and their analogs do not share a core structure. For example Xaa-Pro-dipeptide is structurally distinct from pyrrolidine, piperidine, thiazolidine and their derivatives and other cyclic amines. Therefore, unity of invention is broken.

Election of Species

9. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

10. The species are as follows:

Different DP-IV inhibitors: Xaa-Pro-dipeptides, corresponding derivatives, dipeptide phosphonic acid diaryl esters, dipeptide boronic acids, and their salts, Xaa-Xaa-(Trp)-Pro-(Xaa)n peptides, corresponding derivatives and salts, amino acid amides (Ne-4-nitrobenzyl-oxycarbonyl-L-lysine, L-tryptophan, L-isoleucine, L-valine, and cyclic amines (pyrrolidines, piperidine, thiazolidine and their derivatives, TSL or TMC-2A;

Different inhibitors of APN: actinonin, leuhistin, phebestin, amastatin, bestatin, probestin, b-amino thiols, a-amino phosphonic acid, a-amino phosphinic acid derivatives, and their salts;

Different diseases: benign fibrotic and sclerotic diseases, malign fibroblast hyperproliferation states, fibrotic autoimmune diseases, dermatosclerosis, vitiligo, or heterogeneous group of pseudosclerodermiae and other diseases disclosed in claim 5;

Different systemic application: oral, transdermal, percutaneous, intravenous, subcutaneous, intracutaneous, intramuscular, rectal, vaginal, sublingual administration;

Different topical application form: creams, ointments, pastes, gels, solutions, sprays, liposomes or nanosomes, "pegylated" formulations, degradable depot matrices, mixable lotions, hydrocolloid dressings, plasters, microsponges, prepolymers or other dermatological bases/vehicles.

11. Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

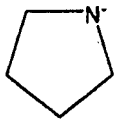
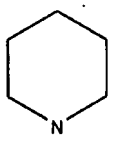
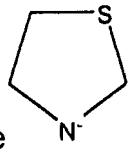
12. For any group elected, Applicant is required to elect a single disclosed species of DP IV inhibitor and APN inhibitor. For examples, the Applicant elects Group I, Applicant elects pyrrolidide as the DP IV inhibitor and amastatine as the APN inhibitor. If Group III is elected, in addition to DP IV inhibitor(s) and APN inhibitor(s), the Applicant is required to elect a single disclosed species of systemic application and if the application is topical, then the form of the topical application. If Group II is elected, in addition to the DP IV inhibitor and APN inhibitor, Applicant is required to elect a single disclosed disease. Please note, if DP IV inhibitor is one of the salts, Applicant is required to elect a single disclosed salt sequence encompasses by the Xaa variables to arrive at a single disclosed salt or derivative species. Please also note, if APN inhibitor is one of the salts, Applicant is required to elect a single disclosed salt species.

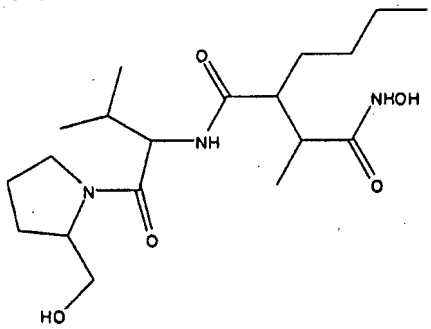
13. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

14. The claims are deemed to correspond to the species listed above in the following manner:

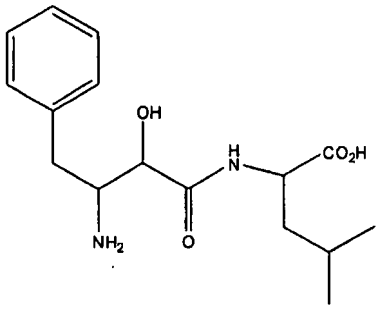
Claims 2-5, 7-9, 11-12, 14.

The following claim(s) are generic: 1, 6, 10, 13 and 15-17.

15. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The DP IV inhibitors are patentably independent and distinct because they have different structures. For example, pyrrolidide has the structure  whereas, the piperidide has the structure  and thiazolidide has the structure  . Search for one would not lead to the other. The APN inhibitors are patentably independent and distinct because they have different structures. For example, actinonin has the structure



while bestatin has the structure



. Further, search for one would not lead to the other. Different systemic application is patentably independent and distinct because of the route of administration. For example, oral is through oral cavity, such as liquid and solid items, while transdermal application is topical, such as cream and paste, and rectal and vaginal applications are through suppositories. Search for on would not lead to the other. Different topical application is patentably independent and distinct because of the different compositions. For example, sprays may contain alcohols and liposomes contains phospholipids to carry drugs through the body, while creams and ointments

may not contain alcohols or liposomes, and are only for topical use. Search for one would not lead to the other. Diseases are patentably independent and distinct because of the cells that the diseases target and the symptoms of the diseases. Further, search for one would not lead to the other.

16. Applicant is advised that the reply to this requirement to be complete must include (i) an election of species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

17. The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

18. **Should applicant traverse on the grounds that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 102(a) of the other invention.**

19. Applicant is reminded that upon the cancellation of claims to non-elected invention, the inventorship must be amended in compliance CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b)(and by the fee required under 37 CFR 1.17(i).

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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11/2/09
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